II. The Claims Are Not Obvious Under 35 U.S.C. § 103

A. Claims 27, 34-36, 38, 40, 41, and 48-49 Are Patentable Over French in View of Mullenbach

Claims 27, 34-36, 38, 40, 41, and 48-49 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 6,290,949 to French *et al.* ("French") in view of Mullenbach *et al.*, UCLA Symp. Mol. Cell. Biol., New Ser., 82:313-326 (1988) ("Mullenbach".) (Office Action, pages 2-3.) Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness, the Office must demonstrate that there is some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine reference teachings. In the present case, the Office has failed to make a *prima facie* case of obviousness because at least this criterion has not been met.

The suggestion to combine or modify the prior art teachings must be clear and particular. *See In re Dembiczak,* 175 F.3d 994, 999 (Fed. Cir. 1999). Thus, while a person of ordinary skill in the art may possess the requisite knowledge and ability to modify the prior art, that modification is not obvious unless the prior art suggested the desirability of such a modification. *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984). Furthermore, the Office has the burden to provide some objective evidence, not found in the Applicants' specification, or reasoned argument showing that one of ordinary skill in the art would have been motivated to combine the prior art to devise the claimed invention. *In re Lee*, 277 F.3d 1338, 1433 (Fed. Cir. 2002).

Applicants submit that the Office has failed to establish a *prima facie* case of obviousness because there simply is no clear and particular suggestion in the cited

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references to combine the adenoviral vector of French with Mullenbach's cDNA encoding glutathione peroxidase. The Office admits that French "does not explicity teach using a sequence encoding a human glutathione peroxidase." (Office Action, page 3.) Then the Office alleges that Mullenbach teaches "the cDNA sequence [of] human glutathione peroxidase." (*Id.*) From this evidence the Office then concludes that one of ordinary skill in the art would have been motivated to combine these references:

> [I]t would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate cDNA encoding a human glutathione peroxidase, taught by Mullenbach et al., into the adenoviral vector (and cells) of French et al. since the patients of the therapy taught in French are primarily human, and using a gene encoding the human protein carries less risk of provoking an immune response against the glutathione peroxidase in humans than would the bovine protein, for example, which is not identical to the human protein.

(*Id.*, emphasis added.) Applicants submit the Office's conclusion that the combination is obvious "since the patients of the therapy taught in French are primarily human, and using a gene encoding the human protein carries less risk of provoking an immune response against the glutathione peroxidase in humans than would the bovine protein" is not based upon sufficient objective evidence or a reasoned argument showing that one of ordinary skill in the art would have been motivated to combine the cited references. For example, French provides only general guidance as to which of the many possible "therapeutic gene sequences" cited therein to choose from (for example, col. 7, line 58, to col. 8, line 26), and provides no guidance regarding relative ability of expressed "therapeutic genes" to provoke an immune response. Further, the Office has not indicated any objective evidence concerning the risk of any glutathione peroxidase provoking an immune

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response. The Office's broad conclusory statement regarding the risk of provoking an immune response is not based upon objective evidence of record or a reasoned argument as is required by *In re Lee*. The mere fact that references can be combined does not render the resulting combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. § 2143.01, citing *In re Mills*, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). Here, Applicants submit that the cited references do not suggest the desirability of combining the adenoviral vectors of French with the cDNA of Mullenbach. The only motivation to combine the references and derive the claimed invention comes from the Applicants' own specification.

In addition, the Office states French teaches that "[t]he adenoviral E1 region is deleted, and all coding sequence[s] may be deleted." (Office Action, page 3.) Applicants point out, however, that the Office has not provided any objective evidence or reasoned argument that the cited references teach or suggest an adenoviral vector wherein an adenoviral E1 gene AND at least one of an adenoviral E2, E4, or L1-L5 genes are not functional. Further, the Office has not indicated how the cited references teach or suggest any non-functional E2, E4, or L1-L5 genes. Accordingly, with regards to at least claim 40, the evidence of record does not indicate how the cited references teach or suggest all of the recited limitations of this claim. For at least this additional reason, claim 40 is not obvious in view of the evidence of record.

In view of these remarks, Applicants respectfully request that the Office reconsider and withdraw the rejection.

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B. Claims 27, 34-36, 38, 40, 41, and 48-50
Are Patentable Over Ohya in View of McClelland

Claims 27, 34-36, 38, 40, 41, and 48-49 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 5,187,078 to Ohya *et al.* ("Ohya") in view of U.S. Patent No. 5,543,328 to McClelland *et al.* ("McClelland".) (Office Action, pages 3-4.) Applicants respectfully traverse this rejection. The Office has failed to establish a *prima facie* case of obviousness since there simply is no clear and particular suggestion in the cited references to combine Ohya's plasmid encoding a glutathione peroxidase with McClelland's recombinant adenoviral vector.

The Federal Circuit has made it clear that a rejection under section 103 cannot rely on reasoning that "presents, in essence, an 'obvious to experiment' standard for obviousness." *In re Dow Chemical Co. v. American Cyanamid Co.,* 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988). Such a standard "would not only be contrary to statute but result in a marked deterioration of the entire patent system..." *In re Thomlinson*, 150 U.S.P.Q. 623, 626 (C.C.P.A. 1966).

The Federal Circuit has given some examples of what would constitute an "obvious to experiment" or "obvious to try" modification based on the prior art:

> In some cases, what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In others, what was 'obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it."

(*In re O'Farrell*, 7 U.S.P.Q.2d 1673 at 1681 (Fed. Cir. 1988) (citations omitted) (emphasis added).)

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The Office's rationale for combining Ohya and McClelland appears to be based upon an impermissible selective "picking and choosing" of specific components. The Office admits that Ohya "does not teach [making] a replication deficient adenoviral vector for this purpose" and then concludes:

> [I]t would have been obvious to one of ordinary skill in the art to have made an adenoviral vector of McClelland al. carrying the human glutathione peroxidase of Ohya et al. for transfecting cultured mammalian cells for the production of the glutathione peroxidase since McClelland et al. taught that the adenoviral vectors were useful for the purpose disclosed in Ohya et al. and were advantageous for such a purpose.

(Office Action, page 4.) Applicants point out, however, that the Office previously admitted that McClelland is deficient because McClelland "does not teach that glutathione peroxidase is a protein of interest." (Office Action dated January 21, 1998, page 21.) Accordingly, Applicants contend that McClelland could not possibly specifically teach that McClelland's adenoviral vectors are useful for Ohya's purpose of transfecting cultured mammalian cells for the production of the glutathione peroxidase. At most, McClelland only provides "general guidance as to the particular form of the claimed invention or how to achieve it." (*In re O'Farrell*, 7 U.S.P.Q.2d 1673 at 1681 (Fed. Cir. 1988 (emphasis added).) At best, the disclosure of McClelland, with the recitation "DNA sequences encoding therapeutic agents," only provides general guidance for the present invention. The cited references fail to provide the desirability leading one of ordinary skill in the art to formulate a recombinant adenovirus comprising a nucleic acid encoding a human glutathione peroxidase. The Office is employing an impermissible "obvious to try" standard of in suggesting that it would have been obvious to combine the Ohya's plasmid encoding a glutathione peroxidase with McClelland's recombinant adenoviral vector.

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As the use of a recombinant adenovirus that comprises a nucleic acid encoding a human glutathione peroxidase would be, at best, "obvious to try" or "obvious to experiment," in the claimed invention, the rejection is improper. Applicants respectfully request reconsideration and withdrawal of the rejection.

SUMMARY

In view of the above remarks, Applicants submit that this application is in condition for allowance. An early and favorable action is earnestly solicited.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

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